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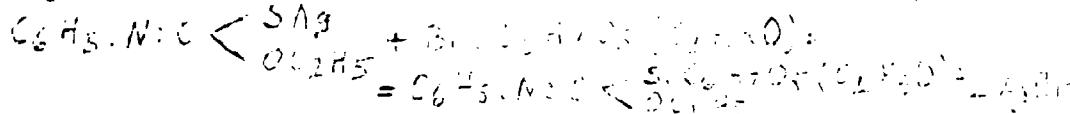
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Investigations of mustard oil glycosides. IV. Phenyl-thiourethane-d-glycoside.

by Wilhelm Schneider and Douglas Clibben.

Erichte d. Deutschen Chem. Ges. Vol 47 (1914), pp 2218-2224.

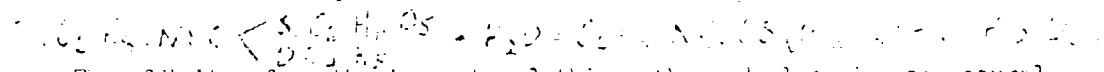
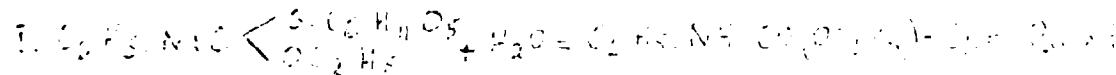
Similarly to the silver salts of other thiourethanes (1), phenyl-thiourethane silver isolated by liebermann (2) also reacts with aceto-bromo-glucose, forming a tetracetyl-thio-urethane-glycoside corresponding to the equation:



However, upon saponification of the acetyl groups with barium hydroxide solution, the primary product phenyl-thiourethane-d-glycoside decomposes, under the effect of aqueous alkali, (similarly to the thiourethane-glycosides described previously,) to phenyl-urethane and the decomposition products of thioglucose.

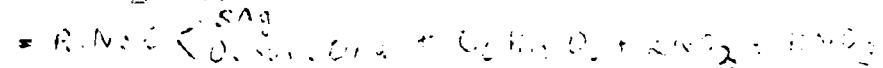
If saponification is effected by means of alcoholic ammonia, a syrupy reaction product is obtained which, in addition to acetamide, contains only totally undecomposed phenyl-thiourethane-d-glycoside, of which unequivocal proof can be submitted. In spite of numerous attempts, we have not been able to obtain the glycoside in crystalline form, although it is a very stable compound upon complete occlusion of water.

Particular interest is offered by the decomposition to which phenyl-thiourethane-d-glycoside is subjected by the influence of water and acids. It assumes here, as it does in respect to its stability, a median position between thiourethane-glycosides synthesized to date on one hand, and the natural mustard oil glycosides (sinigrin, gluco-cheirolin) on the other. While thiourethane-glycosides, aliphatically substituted in connection with nitrogen, decompose and form urethanes and thioglucose, mustard oil glycosides have to date yielded only a cleavage into glucose on one hand, and mustard oil (or its decomposition products) and potassium bisulfate on the other. The hydrolysis of phenyl-thiourethane-d-glycoside progresses in two parallel directions, once likewise with formation of phenylurethane and thioglucose in the sense of equation I, but simultaneously, and similarly to the decomposition of mustard oil glycoside, accompanied by separation of sulfur from the sugar, resulting in the reconstitution of phenyl-thiourethane according to equation II:

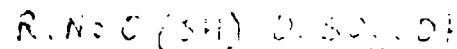


The affinity of synthesized phenyl-thiourethane-d-glycoside to natural mustard oil glycosides is shown with particular clarity by its reaction with silver nitrate. It should be remembered that mustard oil glycosides, upon

treatment with this reagent, yield mustard oil silver sulfates in addition to glucose (3), a process formulated by Gadamer in the following manner:



Phenyl-thiourethane-d-glycoside, upon identical treatment, yields the silver salt of thioglucose on one hand, which immediately separates from the alcoholic-aqueous reaction solution accompanied by the liberation of free nitric acid, but it also reconstitutes phenyl-thiourethane silver, which naturally separates only after neutralization of the nitric acid by an excess of ammonia. The reformation of phenyl-thiourethane-silver must be regarded as being parallel to the formation of mustard oil silver sulfates, with the exception that the latter, due to the acid nature of the sulphydryl group in the hypothetical acids on which they are based,

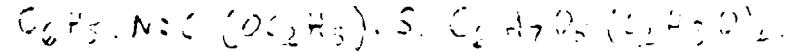


may already form in the acid solution.

The assumption that the constitution of natural mustard oil glycosides in the sense of Gadamer's sinigrin formula may be derived from a hypothetical imino-thiol-carbonic acid, receives considerable support from the present investigation. The stability of glycosides of this type as well as the mode of their hydrolytic decomposition seems to be in close correlation with the more or less acid character of the substitutes which, in addition to the sugar molecule, are attached to the imino-thiol-carbonic acid complex.

Experimental part.

Tetraacetyl-phenyl-thiourethane-d-glycoside,



The silver salt necessary for the synthesis of this compound was produced according to Liebermann's (4) instructions. It differs from the silver salts of other thiourethanes by its poor solubility in chloroform, even at the latter's boiling point. It dissolves easily in higher-boiling halogen hydrocarbons, such as bromobenzene and tetrachloroacetyls, from which it separates in small needles upon cooling, which melt at 206°C (uncorrected) accompanied by decomposition. The compound also dissolves to some extent in boiling benzene, rather easily in boiling toluene, very easily in boiling xylene. It is insoluble in alcohol, ether and water.

20 g phenyl-thiourethane silver were dissolved in 200 ccm boiling xylene and mixed with a hot solution of 28.6 g beta-aceto-bromo-glucose in 100 ccm xylene. After about 3/4 of an hour of boiling on the oil bath the hot solution was separated from the precipitated silver bromide by filtration. Upon cooling, tetraacetyl-phenyl-thiourethane-d-glycoside fell out directly in the form of colorless crystals, which were drawn off by suction and washed with alcohol. The yield amounted to 22 g acetyl glycoside with a melting point of

158°C, corresponding to 62% of the theory.

The pure compound, recrystallized from hot alcohol, melts sharply at 159°C (uncorrected). It is insoluble in water, also in cold ligroin, benzene, toluene, xylene and alcohol, but dissolves easily in ether, chloroform and in hot alcohol and xylene. Reactions with alkaline lead solution and rehling's solution are the same as those of other acetyl-thiourethane-glycosides (5) described heretofore.

0.276 g substance + 0.147 g BaS₂ = 0.323 g BaS₂.

0.2337 g substance + 0.1037 g BaS₂ = 0.3374 g BaS₂.

C₂₅H₂₉O₁₀NS Calculated: C 53.78, H 5.77, S 6.31

Found: C 53.69, H 5.47, S 6.40.

The optical determination was made with the solution in acetylene tetrachloride.

For sodium light, alpha at 15°C equals -0.22° (2 dm tube, concentration 4.4650).

Therefore $[\alpha]_D^{25} = -2.43^\circ$.

Saponification of tetraacetyl-phenyl-thiourethane-d-glycoside.

a) With baryta water: The effect of baryta water alone on tetraacetyl-glycoside is extraordinarily slow; it is speeded up somewhat by the addition of a little alcohol to the suspension of the acetyl-glycoside. 5 g of acetyl compound were shaken for 2 days with a solution of 16 g crystallized barium hydroxide in 200 ccm water and 100 ccm alcohol. The resulting clear solution was separated from excess baryta by means of carbonic acid and concentrated under reduced pressure at 30°C. After removal of alcohol by distillation, a brown oil, soluble in ether, was obtained. The ethereal solution, after evaporation, yielded 0.7 g of a dark oil, which set in crystalline form after standing for several days. The crystals were recrystallized from low boiling ligroin. They were free of sulfur and melted sharply at 52°C (uncorrected), therefore consisted of phenyl-urethane. The aqueous mother liquor of saponification, extracted with ether, developed hydrogen sulfide upon acidification, which evidently had formed by decomposition of primary thioglucose with alkali.

b) With alcoholic ammonia. 5 g acetyl-glycoside were dissolved in 400 ccm hot absolute alcohol. The solution, after cooling to 0°C, was saturated with dry ammonia gas under occlusion of moisture. The acetyl-glycoside which had initially separated in fine-crystalline form during cooling, now dissolved in a clear solution within a few hours, aided by occasional agitation. The solution now rested for 2 days at room temperature, then was freed of dissolved ammonia at the vacuum pump. Subsequent to evaporation of the alcohol under low pressure, a syrupy residue was obtained, which could not be transformed into a crystalline product by any method. The non-alcoholic syrup is insoluble

in ether, but is very easily dissolved with a little alcohol. In this concentrated alcoholic solution, however, even a large admixture of ether cannot cause significant separation. The syrup dissolves easily in water, and quite clearly, if it is freshly produced or stored under strict exclusion of humidity. This shows that the syrup contains, in addition to acetamide, only totally undecomposed phenyl-thiourethane-d-glycoside, since otherwise water-insoluble decomposition products would be visible. The syrup proved to be dextrorotatory in the polarization apparatus.

hydrolysis of
phenyl-thiourethane-d-glycoside.

The clear aqueous solution of the syrupy acetamide-glycoside mixture gradually becomes turbid upon standing at room temperature, and deposits an oily emulsion which settles after a few hours. After a longer period of standing, small amounts of phenyl-thiourethane with a melting point of 72°C (uncorrected) crystallize from the aqueous solution above the oil. As the following test will prove, the oil consists of phenyl-urethane, whose crystallization is prevented by the admixture of a little thiourethane.

The syrupy saponification product from 5 g tetraacetyl-phenylthiourethane-d-glycoside was dissolved in 100 ccm water and allowed to stand at room temperature for 2 days. The oily deposit was absorbed in ether together with the crystalline sediment. After evaporation, the ether yielded about 1.5 g of an oily residue that was dissolved in about 100 ccm of 80% alcohol. By the addition of a sufficient amount of ammoniacal silver solution, phenyl-thiourethane was separated as silver salt which gradually crystallized in the form of needles. It melted at 206°C (uncorrected) and amounted to 0.3 g, corresponding to about 0.16 g phenylthiourethane. The alcoholic mother liquor was freed of alcoholic content under reduced pressure, the residue was absorbed with ether, dried, and isolated by separation from ether. Thus about 1.3 g of an oil were obtained which rapidly solidified in crystalline form after inoculation with a crystal of phenylurethane. The crystalline mass was recrystallized from petroleum ether and the compound identified by its melting point as phenyl-urethane. In the original aqueous glycoside solution, freed with ether of urethane and thiourethane, the presence of thioglucose as the cleavage product corresponding to phenyl-urethane could be proved by the addition of ammoniacal silver solution and much alcohol, the silver salt of which was separated in this manner in the characteristic, amorphous, yellow, easily water-soluble flakes.

Upon boiling with diluted acids the hydrolysis of phenyl-thiourethane-d-glycoside progresses similarly, but much faster. However, phenyl-thiourethane seems to be produced in preponderant amounts, since the obtained water-insoluble oil solidified rapidly into crystals during cooling, which melted directly at 70-71°C. The direction in which phenyl-thiourethane-d-glycoside is predominantly split during hydrolysis, apparently depends on the reaction of its aqueous solution. In alkaline solution (see baryta saponification) only phenylurethane was observed as sugar-free cleavage product. In aqueous solution urethane and thiourethane are obtained simultaneously; in acid solution, primarily phenyl-thiourethane (6).

The enzyme myrosin, which splits mustard oil glycosides, significantly has no noticeable effect on phenyl-thiourethane-d-glycoside. In two parallel tests, in which equal quantities of glycoside were subjected to aqueous hydrolysis under otherwise identical conditions, once without, once with admixture of myrosin solution, the amounts of oily decomposition products extracted from time to time with ether, were quantitatively equal.

Reaction of
phenyl-thiourethane-d-glycoside
with silver nitrate.

The saponification product of tetraacetyl-phenyl-thiourethane-d-glycoside was dissolved in 100 ccm of 80% alcohol and mixed with 16 ccm silver nitrate solution (1:10). After a short time thioglucose silver separated in the form of an amorphous, brown powder. The solution was stored in the refrigerator for 4 hours to complete the reaction. Subsequently the separated powder was drawn off by suction through a layer of siliceous earth and decomposed by introduction of hydrogen sulfide. After filtration from the silver sulfide precipitate, a colorless, aqueous solution was obtained, which was completely freed of dissolved hydrogen sulfide at the vacuum pump. After the addition of 3 ccm of an ammoniacal silver nitrate solution (1:10), thioglucose silver separated in purified form. It formed snow-white, amorphous flakes which during sedimentation turned slightly yellowish. The remaining liquid was poured off, the precipitate was again decanted with 100 ccm 80% alcohol and finally drawn off by suction. The preparation was first dried for one day in vacuo over phosphorous pentoxide, then to constant weight at the temperature of chloroform vapor. The yield amounted to 0.46 g. The silver-thioglucose thus obtained represented a weakly yellowish, amorphous, very stable powder, which even withstood extended heating at 100°C (water steam) without apparent change. When heated in the melting point apparatus, it gradually turned brown at above 100°C and melted at about 165°C after turning black. It could be demonstrated that the increased stability of this preparation as compared to previously described ones (7) is attributable to the circumstance that an excess of silver solution had been avoided in the precipitation of thioglucose; on the contrary, too little silver had been used. Even in aqueous solution this preparation was quite stable, it even withstood short boiling, whereby more intensive yellowing only developed very slowly. However, a trace of excessive silver salt solution caused rapid decomposition even at room temperature, accompanied by blackening, of the aqueous solution of thioglucose-silver, as well as of the flakey suspension freshly precipitated therefrom with alcohol. The preparation was entirely free of nitrogen; nevertheless the silver content was found to be about 2% too low, similarly to previous experience, while the sulfur content agreed well with the formula for thioglucose silver. This result probably can be explained most simply by saying that the silver compound had adsorbed and carried over a small quantity of thioglucose (or some disulfide resulting therefrom).

0.46 g substance : 0.0373 g AgNO_3 , 0.155 g S

$C_6H_{11}O_5S\text{Ag}$. Calculated: S 10.55, Ag 35.3%
Found: S 10.55, Ag 33.45%

The original, silver nitrate-containing reaction mixture, filtered off from crude thioglucose silver, was mixed with an excess of ammonia. Soon copious quantities of phenyl-thiourethane silver crystals separated out, which were identified by their solubility and melting point. Hence it follows that, in the presence of silver nitrate, the decomposition of phenyl-thiourethane-d-glycoside takes place in both of two possible directions.

NOTES

- (1) Cf. W. Schneider, D. Clibben, G. Hullweck and W. Steibelt, Vol. 47, 1258 (1914).
- (2) Paper 207, 142 (1881).
- (3) Gadamer, paper 235, 47 and following (1897); W. Schneider and L.A. Schuetz, Vol. 46, 2634 (1913).
- (4) Paper 207, 142 (1881).
- (5) Vol. 47, 1261 and following (1914).
- (6) To a certain degree, sinigrin reacts similarly. Silver nitrate in aqueous solution (i.e. in a solution which rapidly turns acid owing to freed nitric acid) produces from it only allyl-mustard oil silver sulfate and glucose. Through the effect of alcoholic ammonia, a small amount of thioglucose results as the decomposition product of this natural mustard oil glycoside. Cf. the following paper.
- (7) See Vol. 47, 1263, 1265, 1268 (1914).